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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,581	02/22/2001	Paolo Mascagni	205,042	9301

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EXAMINER

MAIER, LEIGH C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 02/12/2003

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/763,581

Applicant(s)
Mascagni

Examiner
Leigh Maier

Art Unit
1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Nov 26, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above, claim(s) 15-25 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14, 26, and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3 6) ☐ Other:

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DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-14, 26, and 27, in Paper No. 5 is acknowledged.

Claim Objections

Claim 8 is objected to because of the following informalities: "Heptakis" is misspelled (3 times). Appropriate correction is required.

Claims 1-14, 26, and 27 are objected to for use of non-standard terminology in claiming a Markush group of paroxetine/cyclodextrin complexes. For Applicant's consideration, a more acceptable wording of the independent claim, with no change in scope, would be "*A complex of paroxetine, as a free base or as a salt, with a cyclodextrin or with a cyclodextrin derivative.*"

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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The terms "high solubility" in claim 2 is a relative term which renders the claim indefinite. The term "high solubility" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Further regarding this claim, the claim recites that the complexes are characterized by "chemical stability." However it is well known that many chemical compounds are stable under some conditions and not others. The specification does not supply any guidance as to the conditions contemplated. The specification only discusses "greater stability in comparison with the non-complexed product." See page 7, line 13.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 6-14 are rejected under 35 U.S.C. 102(b) as being anticipated by RONSEN et al (WO 99/16440).

RONSEN et al (WO 99/16440) discloses a free-flowing complex of paroxetine HCl and hydroxypropyl- β -cyclodextrin. See example 5. The reference is silent regarding (1) the ultimate

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molar ratio of the paroxetine and (2) the cyclodextrin derivative presence or absence of ethanol in complex. However, the reference states that the product is dried under vacuum. Furthermore, given the starting molar ratio in the example, it would appear that the ratio of the final product would be about 1:1 and fall into the broad range recited in claims 13 and 14. Since the Office does not have the facilities for preparing the claimed materials and comparing them with prior art inventions, the burden is on Applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.d. 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald*, 619 F.d. 67, 205 USPO 594 (CCPA 1980).

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-14, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over RONSEN et al (WO 99/16440).

The claims are drawn to a Markush group of paroxetine/cyclodextrin complexes. Dependents recite limitations regarding particular cyclodextrin species, molar ratios of the components, and pharmaceutical compositions comprising the complexes.

RONSEN teaches as set forth above. The reference does not exemplify the preparation of complexes using the full range of cyclodextrins recited in the claims. The reference does not explicitly teach a pharmaceutical composition comprising the exemplified paroxetine/cyclodextrin complex and an excipient.

Regarding cyclodextrin derivative and molar ratios, RONSEN exemplifies the use of β -HP-cyclodextrin, but also teaches that other cyclodextrins (α - and γ -) and other derivatives. See page 6, lines 16-24. It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the paroxetine complex with any known cyclodextrin for the art-disclosed utility. It would be within the scope of the artisan to optimize the molar ratio through routine experimentation.

Regarding pharmaceutical compositions, the reference teaches the preparation of pharmaceutical compositions comprising other paroxetine/hydroxyl-bearing compounds. See

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example 10. It would have been obvious to one having ordinary skill in the art to prepare a pharmaceutical composition comprising the exemplified paroxetine/cyclodextrin complex and an excipient for its art-disclosed utility as an SSRI antidepressant. See page 1.

Claims 4, 5, 10, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over RONSEN et al (WO 99/16440) as applied to claims 1-3, 6-9, and 12-14 above, and further in view of BENNEKER et al (US 5,874,447).

The invention is as set forth above. Dependents recite the presence of water in the complex and species of acid used to prepare the paroxetine salt.

RONSEN teaches as set forth above. The reference does not teach the use of acids other than HCl to prepare the a paroxetine salt or the use of the free base. The reference is silent regarding the presence of water. However, the reference does note the utility of hydrates of paroxetine. See page 2, lines 15-17. RONSEN teaches that complexation of the paroxetine with a hydroxyl-bearing compound produces more easily handled non-hygroscopic, amorphous product. See page 2, lines 21-34.

BENNEKER teaches paroxetine free base and a number of paroxetine salts, including maleate, acetate, and methanesulfonate. The reference further teaches hydrates of the paroxetine derivatives. See col 5-6.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a cyclodextrin complex of the free base of paroxetine or any

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known salt thereof for the enhanced physical properties derived from complexation. Furthermore, the use of known multi-hydrate would provide the presence of water required in the claims.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Tuesday, Wednesday, or Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at <http://www.uspto.gov>. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.



Leigh C. Maier
Patent Examiner
February 6, 2003